UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,358	03/09/2001	Robert A. Ach	10971722-2	7724

7590 12/04/2002

AGILENT TECHNOLOGIES, INC.
Legal Department, 51UPD
Intellectual Property Administration
P.O. Box 58043
Santa Clara, CA 95052-8043

EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/04/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/802,358	Ach
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 5, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *17-20 and 24-44* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17-20 and 24-44* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claim 19 has been amended. Non-elected claims 21-23 have been canceled without prejudice towards further prosecution. New claims 24-44 have been added.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 17-20, 24, 25, 26, 28-32, and 36-41 are rejected under 35 U.S.C. 103(a) over Martin et al. (RNA, (1998), Vol. 4, pages 226-230) in view of Cao et al. (Proceedings of the National Academy of Sciences, (USA), (1996), Vol. 93, pages 11580-11585) further in view of Stratagene Catalog (1988, page 39).

Martin et al teach the reagents and methods for end-labeling ribonucleic acids with non-radioactively labeled ribonucleotides comprising:

a non-radioactively labeled ribonucleotide which is directly detectable ; and

an eukaryotic poly(A) polymerase (Abstract and RESULTS and DISCUSSION Section, Labeling of RNA with nonradioactive nucleotides Subsection, and Figures 1-4).

Martin et al teach the reagents and methods, wherein the non-radioactively labeled ribonucleotide is a non-radioactively labeled ATP and UTP analog (Abstract).

Martin et al teach the reagents and methods, wherein the non-radioactively labeled ribonucleotide is fluorescently labeled with fluorophore fluorescein (Abstract and RESULTS and DISCUSSION Section, Labeling of RNA with nonradioactive nucleotides Subsection).

Martin et al do not teach the reagents and methods, wherein the prokaryotic poly(A) polymerase is a bacterial polymerase Escherichia coli poly(a) polymerase 1 or 2.

Cao et al. teach the reagents and methods, wherein the prokaryotic poly(A) polymerase is a bacterial polymerase Escherichia coli poly(a) polymerase 1 or 2 (Abstract and MATERIALS AND METHODS and Figures 1-5).

It would have been further *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the reagents and methods, wherein the prokaryotic poly(A) polymerase is a bacterial polymerase of Cao et al. into the composition of Martin et al, since Cao et al. state, "The identification of the gene for the second E. Coli. poly(A) polymerase opens the way for the detailed investigation of the metabolic role of mRNA polyadenylation by studying the consequences of disruption of either or both of the poly(A) polymerase genes (Page 11585, Column 2, last sentence)". By employing scientific reasoning, an ordinary artisan would have combined and substituted a functional equivalent poly(A) polymerase of Cao et al. into the composition of Martin et al, in order to improve the detailed investigation of the metabolic role of mRNA polyadenylation. An ordinary practitioner would

have been motivated to combine and substitute the reagents and methods, wherein the functional equivalent prokaryotic poly(A) polymerase is a bacterial polymerase of Cao et al. into the composition of Martin et al, in order to achieve the express advantages , as noted by Cao et al., of an invention which provides the detailed investigation of the metabolic role of mRNA polyadenylation by studying the consequences of disruption of either or both of the poly(A) polymerase genes.

Martin et al. in view of Cao et al. do not teach the motivation to combine all the reagents for end-labeling a ribonucleotide in the form of a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a suitable container, non-radioactively labeled ribonucleotide and a prokaryotic poly(A) polymerase of Martin et al. in view of Cao et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually

need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control (page 39, column 1).

4. Claims 27, 34, 35, 42- 44 are rejected under 35 U.S.C. 103(a) over Martin et al. (RNA, (1998), Vol. 4, pages 226-230) in view of Cao et al. (Proceedings of the National Academy of Sciences, (USA), (1996), Vol. 93, pages 11580-11585) further in view of Stratagene Catalog (1988, page 39) further in view of Waggoner et al. (U.S. Patent 6,479,303 B1) (November 12, 2002).

Martin et al. in view of Cao et al. further in view of Stratagene Catalog teach the method of claims 17-20, 24, 25, 26, 28-32, and 36-41 as described above.

Martin et al. in view of Cao et al. further in view of Stratagene Catalog do not teach the method, wherein the polymethine fluorophore is a cyanine fluorophore chosen from Cy3, cy5, and Cy7.

Waggoner et al. teach the method, wherein the polymethine fluorophore is a cyanine fluorophore chosen from Cy3, cy5, and Cy7 (Abstract, Column 11, lines 42-60 and Table 1).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the reagents and methods, wherein the polymethine fluorophore is a cyanine fluorophore chosen from Cy3, cy5, and Cy7 of Waggoner et al. into the composition of Martin et al in view of Cao et al. further in view of Stratagene Catalog since Waggoner et al. states, "The development of such multichromophore complexes is

particularly useful for multicolor detection systems (Column 11, lines 58-60)". An ordinary practitioner would have been motivated to combine and substitute the reagents and methods, wherein the polymethine fluorophore is a cyanine fluorophore chosen from Cy3, cy5, and Cy7 of Waggoner et al. into the composition of Martin et al in view of Cao et al. further in view of Stratagene Catalog in order to achieve the express advantages , as noted by Waggoner et al., of an invention which provides the development of multichromophore complexes particularly useful for multicolor detection systems.

Response to Amendment

5. In response to amendment, previous 103(a) rejection has been maintained along with a new 103(a) rejection.

Response to Arguments

6. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence

of strong motivation provided by Cao et al since Cao et al states, "The identification of the gene for the second E. Coli. poly(A) polymerase opens the way for the detailed investigation of the metabolic role of mRNA polyadenylation by studying the consequences of disruption of either or both of the poly(A) polymerase genes (Page 11585, Column 2, last sentence)". Similar logic is applicable to other combination of references.

Applicant is also hereby notified in response to the arguments that the failure of Rosenmeyer et al. (U.S. Patent 5,573,913) (November 12, 1996) to end-label a ribonucleic acid with a non-radioactively labeled ribonucleic acid and a poly(A) polymerase is not persuasive. Applicant also argues that there is a structural difference between prokaryotic and eukaryotic polymerase, especially applicant refers to an upstream consensus sequence such as the AAUAAA which prokaryotic polymerase does not require for its function. This argument is not persuasive, especially in the absence of any disclosure in the specification or in the claim of the instant invention that an upstream consensus sequence such as the AAUAAA has any effect or any role to play in the end-labeling of ribonucleic acid with a non-radioactive label. Applicant is hereby notified that function of an enzyme and end-labeling of a substrate of that enzyme are two completely different phenomenon. Moreover, Martin et al (as cited above) clearly teaches to successfully end-label a ribonucleic acid with a non-radioactively labeled ribonucleic acid and a poly(A) polymerase.

Applicant then argues the 103 rejection is improper because it lacks a reasonable expectation of success.

With regard to the "lack of reasonable expectation of success" argument, The MPEP 2143.02 states

"Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart , 531 F.2d 1048, 189 USPQ 143 (CCPA 1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also Amgen, Inc. v. Chugai Pharmaceutical Co ., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied , 502 U.S. 856 (1991) (In the context of a biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); In re O'Farrell , 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.)."

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Martin reference of the enabling methodology, the suggestion to modify the prior art, and evidence that a number of different poly(a) polymerase from Escheirchia coli were fluorescently labeled and were actually experimentally studied and found to be functional (Example 7). This evidence of functionality trumps the attorney arguments, which argues that Martin reference is an invitation to research, since Mertin steps beyond research and shows the functional product.

Accordingly, all previous 103(a) rejection along with a new 103(a) rejection is hereby properly maintained.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

Arun Chakrabarti,

Patent Examiner,

November 18, 2002